CURRENT LITERATURE

SUBARACHNOID HEMORRHAGE AS A CAUSE OF EPILEPSY

Predictors and Clinical Impact of Epilepsy after Subarachnoid Hemorrhage

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PURPOSE: To determine the frequency, predictors, and impact on outcome of epilepsy developing during the first year after subarachnoid hemorrhage (SAH).

METHODS: The authors prospectively analyzed 247 of 431 patients with SAH treated over a period of 5 years who were alive with follow-up at 12 months. Epilepsy was defined as two or more unprovoked seizures after hospital discharge.

RESULTS: New-onset epilepsy occurred in 7% ($n = 17$) of patients; an additional 4% ($n = 10$) had only one seizure after discharge. Independent predictors of epilepsy included subdural hematoma [odds ration (OR 9.9; 95% confidence interval (CI), 1.9–52.8] and cerebral infarction (OR, 3.9; 95% CI, 1.4–11.3). Unlike those without seizures, patients who developed epilepsy failed to experience functional recovery on the modified Rankin Scale (mRS) between 3 and 12 months after SAH. At 12 months, epilepsy was independently associated with severe disability (score ≥ 3) on the mRS (OR, 10.3; 95% CI, 2.5–42.0), increased instrumental disability on the Lawton Instrumental Activities of Daily Living scale (OR, 4.9; 95% CI, 1.1–22.2), reduced quality of life on the Sickness Impact Profile (OR, 4.5; 95% CI, 1.1–18.0), and increased state anxiety on the Spielberger Anxiety Inventory (OR, 4.8; 95% CI, 1.1–20.4). Epilepsy was not associated with cognitive impairment, depression, or subjective life satisfaction.

CONCLUSIONS: Epilepsy occurred in 7% of patients with SAH, was predicted by subdural hematoma and cerebral infarction, and was associated with poor functional recovery and quality of life. Our findings indicate that focal pathology, rather than diffuse injury from hemorrhage, is the principal cause of epilepsy after SAH.

COMMENTARY

The usual concern of neurologists and neurosurgeons with respect to epileptic seizures in patients with subarachnoid hemorrhage (SAH) centers on their potential occurrence after the initial bleed, resulting in increased intracranial pressure, which in turn may lead to a serious rerupture of the aneurysm (1). Such concern has motivated the practice of treating patients prophylactically with phenytoin or phenobarbital. The study by Classen et al. provides a new and different perspective with respect to the significance of epilepsy after SAH; it suggests that epilepsy heralds a poor functional recovery and quality of life of these patients 1 year after the bleed.

The prevalence of epileptic seizures after SAH has ranged between 7% and 12% among various case series (2,3), which is comparable to that reported by Classen among patients who survived 12 months: 7% developed more than two spontaneous seizures, and 4%, a single seizure. Early or "in-hospital" new-onset seizures occurred in 27 (6.4%) patients, with a dismal prognosis, as 19 (70.3%) of these patients were dead at 12 months. Nine of them had nonconvulsive status epilepticus, and eight died. Thus, early seizures after SAH are associated with a high mortality risk. This higher mortality associated with early seizures is found not only among patients with SAH, however; it has been reported in patients with stroke. Indeed, in a British case–control study, mortality in the group with seizures at stroke onset was 4.2 times greater than in the whole stroke group combined in the first 48 hours after stroke (4).

Independent predictors of epilepsy at 12 months included cerebral infarction and subdural hematoma. In the presence of both variables, the risk was as high as 75%. These findings were not surprising, given the well known association of epilepsy and hemorrhagic strokes. The seizure frequency was in general relatively low among the 17 patients with epilepsy alive at 12 months: 59% had experienced only two seizures; 18%, three seizures; and only 24% had reported four or more seizures. Yet the presence of epilepsy was found to be an independent predictor of poor functional recovery at 12 months on a variety of disability instruments, of poor quality of life and state of anxiety. The contrast between the relatively low seizure frequency in almost three fourths of these patients and a poor outcome begs the question: "Is epilepsy playing a pathogenic role in the poor recovery of these patients, or is it an epiphenomenon of a serious CNS insult that resulted in the development of both seizures

and poor recovery among survivors of SAH?" To muddy the waters further, patients with epilepsy did not exhibit a higher prevalence of depression, the one variable that has been repeatedly associated with poor quality-of-life ratings among patients with chronic epilepsy (5). Classen et al. suggested that the use of antiepileptic drugs (AEDs) may interfere with functional recovery. This argument, although attractive from a theoretical standpoint, remains speculative at this point. Thus, the pathogenic role of epilepsy in the long-term outcome of patients with SAH is yet to be established. Nevertheless, the data of this study clearly showed that the risk of epileptic seizures goes beyond the immediate risk of rebleeding; it must serve as a red flag anticipating a difficult recovery.

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References

1. Mohr JP, Kistler JP, Zabramski JM, Spetzler FM, Barnett HJM. Intracranial aneurysms. In: Barnett HJM, Mohr JP, Stein BM, Yatsu FM, eds. Stroke: pathophysiology, diagnosis and management. New York: Churchill Livingstone, 1986:643– 677.
2. Ogden JA, Utley T, Mee EW. Neurological and psychosocial outcome 4 to 7 years after subarachnoid hemorrhage. Neurosurgery 1997;41:25–34.
3. Ukkola V, Heikkinen ER. Epilepsy after operative treatment of ruptured cerebral aneurysms. Acta Neurochir 1990;106:115–118.
4. Shinton RA, Gill JS, Melnick SC, Gupta AK, Beevers DG. The frequency, characteristics and prognosis of epileptic seizures at the onset of stroke. J Neurol Neurosurg Psychaitry 1988;51:2730–2776.
5. Gilliam F. Optimizing epilepsy management, seizure control reduction, tolerability and co-morbidities: introduction. Neurology 2002;(suppl 5):S1.